A Study of Thermal Characteristics of Biological Tissue and Their Application to Medical Diagnosis

著者	岡部 孝裕
号	60
学位授与機関	Tohoku University
学位授与番号	工博第5142号
URL	http://hdl.handle.net/10097/00120473

	おかべ　たかひろ
氏　　　　　名	岡　部　孝　裕
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指　導　教　員	東北大学教授　圓山　重直
論文審査委員	主査　東北大学教授　圓山　重直　東北大学教授　佐藤　岳彦 東北大学教授　早瀬　敏幸　東北大学教授　山家　智之 東北大学准教授　小宮　敦樹　東北大学講師　関　隆志

論 文 内 容 要 旨

Chapter 1:　General introduction and background

In chapter 1, the general introduction and background of this study was described. The importance of thermal characteristics of biological tissues, especially living one, was also introduced. The criteria for its measuring techniques and application to a medical diagnosis were discussed. Consequently, the remaining challenges and objectives of this dissertation: the development of measuring methods for the thermophysical properties of biological tissue, the clinical experiment with human skin, the investigation of blood perfusion effects in human skin and the development of medical diagnosis technique from the viewpoint of thermal characteristics were explained.

Chapter 2:　Fundamentals of thermal characteristics of biological tissues

In chapter 2, the fundamentals of thermal characteristics of biological tissues were explained. Heat transfer in the biological tissues and the bioheat transfer equations were described. Furthermore, particularly-important factors which are the heat loss to the lead wires and the initial temperature distribution in a body for non-invasive method were introduced, and discussed in detail. The consideration in a medical diagnosis was investigated using an analytical solution of Pennes' bioheat transfer equation.

Chapter 3:　Development of inverse method utilizing thermophysical handy tester

In chapter 3, an inverse method utilizing the thermophysical handy tester with newly developed heat conduction model, which can separately estimate the variable vectors such as the thermal conductivity, thermal diffusivity and blood perfusion rate (not apparent value), has been established. The optimization of variable vectors is based on a real-coded genetic algorithm using the unimodal normal distribution crossover. Furthermore, it can include the effect of initial temperature distribution in a body to the calculation. To validate the method, the measurement of thermal conductivity of the standard materials was conducted, and the results showed a good agreement with the reference values. Additionally, *in-vitro* measurement of thermal diffusivity of biomaterials such as meats, fruits and vegetables were conducted. The measureable range of an inverse method was investigated. It indicated that the measurable range was 0.14 - 1.3 W/(m･K), meaning that our method is effective for the measurement of the biological tissues, because the range of thermal conductivity of that is generally lower than 0.60 W/(m･K), which is that of water.

Chapter 4:　Development of accurate temperature probe utilizing guard heater

In chapter 4, the accurate temperature probe for accurately and precisely measuring the skin surface temperature and apparent thermal conductivity has been developed. To overcome the problem in the heat loss through the lead wires when the measurement for a material with higher temperature than the room temperature, a guard heater method was applied to minimize it. The performance evaluation of the accurate temperature probe was done by the measurement of surface temperature and thermal conductivity of a heated material at 35.00ºC using the newly developed a Peltier system to verify whether the heat loss can be successfully minimized. Figure 1 shows the measured result of time variation of temperature in cases with and without guard heating. For the case with guard heating, the precise measurement of surface temperature on a heated aluminum can be successfully achieved. The precision of temperature measurement was approximately ± 5 mK which makes measurement much more precisely than a thermocouple and thermography. On the other hand, for the case without a guard heating, there was a temperature difference from the object temperature of 35.00ºC, which was approximately 0.21ºC due to the heat loss through the lead wires and a tube. Consequently, the thermistor probe utilizing a guard heater could accurately measure the surface temperature of even a heated material despite the contact-based method. The numerical study for the performance evaluation was also done with the calibrated numerical model. It indicated that the accurate temperature probe could accurately and precisely measure the skin surface temperature and apparent thermal conductivity as well as the experimental approach. The meat materials were measured by the accurate temperature probe, the reasonable values with high accuracy came out.

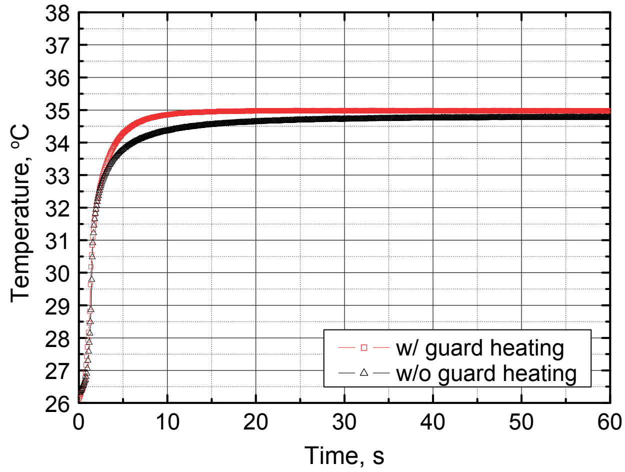

Fig. 1 Time variation of temperature in cases with and without guard heating.

Chapter 5: Investigation of blood perfusion effects in human skin

In chapter 5, the effect of blood perfusion in human skin on the measurement by both the accurate temperature probe and an inverse method were investigated. To clarify the effect of blood perfusion in human skin, the sensitivity analysis for the methods was performed at first. It indicated that the effect of blood perfusion rate by itself and the initial temperature distribution did not significantly affect on both of them at normal condition.

By using an inverse method, the clinical experiments with actual human skin were conducted to estimate the thermal diffusivity. Additionally, an experiment with a corpse who had no physiological effect was also conducted to compare to the clinical experiment with living skin. The results indicated that the estimated values of thermal diffusivity of both living and dead skin in forearm showed a good agreement each other despite the existence of blood flow or not.

By using the accurate temperature probe, the measurements of apparent thermal conductivity of human skin on the back of hand and finger were conducted. As for the case on back of hand, the results showed good repeatability of measurement, and 0.441 ± 0.0024 W/(m·K) which is reasonable. Meanwhile, as for the case on finger, the results could not showed good repeatability due to the fluctuation of baseline temperature caused by the increased blood flow, showing a possibility that the accuracy and precision of accurate temperature probe for the living tissue measurement strongly depend on the location on a body. Moreover, the accurate temperature probe was applied to the indirect detection of increased blood flow during a thermal therapy using the abdominal heater. It

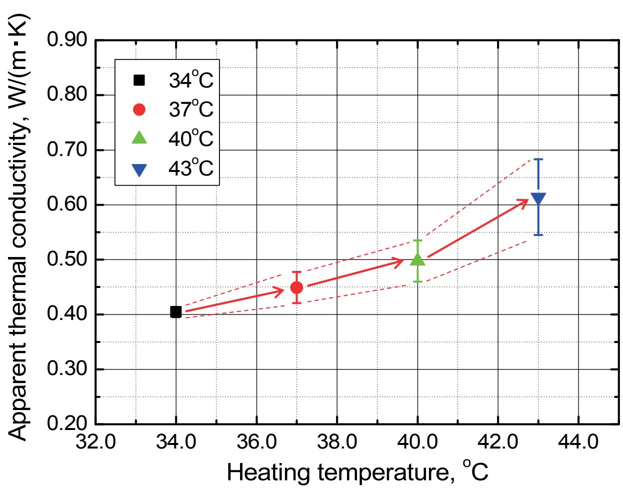

Fig. 2 Relationship between apparent thermal conductivity and heating temperature.

was found in the calculation results that the increase of blood perfusion during a thermal therapy greatly affected on the initial temperature distribution in a body, and then the apparent thermal conductivity was indirectly varied, showing the positive correlation with blood perfusion. Additionally, a clinical experiment with an actual human abdominal area was also conducted to demonstrate a detection of increased blood flow by the measurement of apparent thermal conductivity at heating temperature of 34, 37, 40 and 43°C. Figure 2 shows the relationship between the apparent thermal conductivity and the heating temperature of thermal therapy. The experimental results showed that the mean values of apparent thermal conductivity increased with the heating temperature of thermal therapy, because of the change in the initial temperature distribution with the heating temperature as expected by a numerical approach. Meanwhile, the standard deviation of apparent thermal conductivity measurement also increased with the heating temperature. In this case; however, the increase of blood perfusion at higher heating temperature during thermal therapy caused getting greater of standard deviation.

Chapter 6: Application to medical diagnosis

In chapter 6, the feasibility of the early detection of the malignant melanoma by the accurate temperature probe was investigated both numerically and experimentally. In a numerical study, the feasibility of the early detection of malignant melanoma by the accurate temperature probe was firstly conducted using a 2D axisymmetric model with a variety of Clark level of malignant melanoma and healthy skin. Figure 3 shows the relationship between the apparent thermal conductivity and the volume of malignant melanoma. The calculation results showed that there was a positive correlation between the volume of melanoma and the apparent thermal conductivity, indicating that the accurate temperature probe enables to detect the difference of apparent thermal conductivity between the healthy skin and lesion even if the early stage. An animal experiment was performed to investigate the difference between the healthy skin and lesion. Consequently, it showed the obvious difference between them, but the inverse trend to a numerical calculation was obtained because of the fibrolast in a tumor. The results showed the feasibility to early diagnose the malignant melanoma from the measurement of apparent thermal conductivity by the accurate temperature probe.

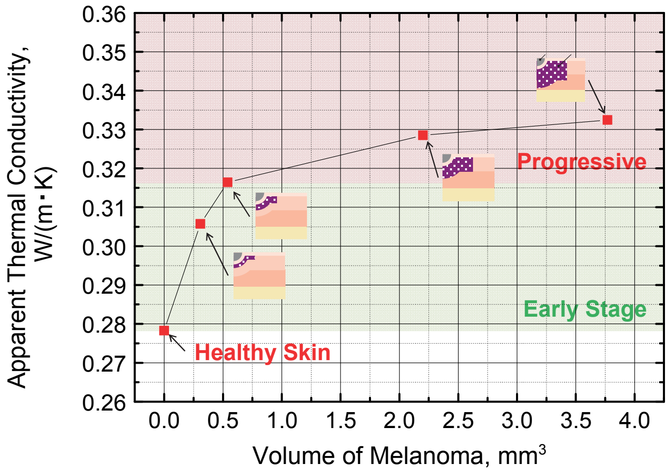

Fig. 3 Relationship between apparent thermal conductivity and volume of malignant melanoma.

Chapter 7: General conclusion

In chapter 7, the conclusions obtained from the each chapter which will contribute to clarification of the heat transfer in biological tissue were summarized. The obtained conclusions were as follows.

1. Two practical methods for measuring thermophysical properties of biological tissues: the inverse method utilizing thermophysical handy tester and the accurate temperature probe utilizing a guard heater were developed and evaluated in this dissertation.
2. The blood perfusion effect in human skin and the effect of initial temperature distribution in a body on the measuring results under the different conditions were clarified by the clinical experiments with actual human skin.
3. The accurate temperature probe was applied to the medical diagnosis for the skin cancer at the early stage from the viewpoint of thermophysical properties. It shows a possibility to detect the difference between the malignant melanoma at the early stage and a benign skin by only measuring the apparent thermal conductivity using the accurate temperature probe.

論文審査結果の要旨

温熱療法やレーザ治療など伝熱現象を用いた治療法は，その侵襲性の低さから注目を集めている。これらの治療法では，より安全に施術するために生体内の温度場の把握や加熱量の定量的評価は重要となる。そこで，数値シミュレーションは有効的な手段であるが，その結果の信頼性はモデルのみならず熱物性値に依存しており，適切な計測が必要となる。本研究では異なるコンセプトを有する二種類の実用的な熱物性計測手法を開発している。さらに，病変部における熱物性や血流の局所的な違いに着目し，開発した一つの手法を新たな皮膚がんの非侵襲早期発見手法に応用している。本論文は，これらの研究成果をまとめたものであり，全編 7 章からなる。

第 1 章は序論であり，本研究の背景，目的および構成を述べている。

第 2 章では，生体内における伝熱現象の基礎と熱物性評価による医療診断の可能性について述べている。また，生体表面から熱物性計測を行う際の問題点である計測センサのリード線への熱損失や生体内初期温度分布について議論している。これらの議論は次章以降において重要な知見である。

第 3 章では，生体の熱物性値（熱伝導率及び熱拡散率）と血流等の影響を独立に推定することを目的とし，固体熱物性テスターを用いた逆問題解析手法の開発を行っている。水などの標準試料や豚の肉などの生体試料の熱物性の推定を行うことによって，手法の妥当性の検証を行っている。これは，非侵襲熱物性評価において重要な成果である。

第 4 章では，生体表面の高精度・高確度な表面温度及び熱伝導率計測を目的とした，保護熱源を有する高精度温度プローブの開発を行っている。また，開発した手法が表面温度及び熱伝導率計測の高い確度と精度を有していることを評価している。これは，皮膚などの生体表面から熱物性計測を行うために有用な成果である。

第 5 章では，第 3 章及び第 4 章で確立した計測手法を用いたヒトの皮膚の臨床実験を行っている。また，それぞれの手法に対して，血流及び初期温度分布が計測結果に与える影響の検証を行っている。血流及び代謝の影響のない死体の皮膚の熱拡散率計測や温熱治療時の皮膚の見かけの熱伝導率計測を行い，様々な条件下での皮膚の熱特性について議論している。これは，様々な環境下における皮膚の熱物性評価及び熱特性解明において重要な知見である。

第 6 章では，第 4 章で確立した計測手法を皮膚がんの早期発見手法へ応用している。数値計算及び動物実験を行い，健常皮膚と病変部の違いを熱的観点から検出できる可能性を示している。これは，本手法の実用化に向けた有用な成果である。

第 7 章は結論である。

以上要するに本論文は，生体組織の熱特性の理解を熱物性値の計測によって深め，医療診断への応用を行ったものであり，機械システムデザイン工学および医工学の発展に寄与するところが少なくない。よって，本論文は博士(工学)の学位論文として合格と認める。